

Atty. Dkt. No. 041673-2047

Listing of Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Currently Amended) A method for ameliorating neuronal atrophy and loss in the mammalian brain, the method comprising delivering a neurotrophin-encoding transgene composition to preselected delivery sites in the brain for expression of the neurotrophin at, or within diffusion distance of, targeted cholinergic or dopaminergic neurons, wherein the neurotrophin is nerve growth factor (NGF) or glial derived nerve growth factor (GDNF) and growth factor stimulates non-chemotropic axonal growth by, or activity in, the targeted neurons.
2. (Cancelled)
3. (Cancelled)
4. (Cancelled)
5. (Cancelled)
6. (Withdrawn) The method according to Claim 1, wherein the neurotrophin-encoding transgene composition is delivered indirectly, from grafts of transgene-secreting donor cells introduced into the brain.
7. (Cancelled)
8. (Cancelled)

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9. (Withdrawn) The method according to Claim 6, wherein the donor cells are delivered in a pharmaceutically acceptable composition having a concentration of at least 1×10^5 donor cells/ μ l.

10. (Withdrawn) The method according to Claim 9, wherein each graft contains from 2 to 20 μ l of the donor cell containing composition.

11. (Cancelled)

12. (Cancelled)

13. (Cancelled)

14. (Cancelled)

15. (Cancelled)

16. (Cancelled)

17. (Cancelled)

18. (Cancelled)

19. (Cancelled)

20. (Cancelled)

21. (Previously Presented) The method according to Claim 1, wherein the targeted neurons are cholinergic neurons.

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22. (Previously Presented) The method according to Claim 21, wherein the stimulation occurs in a cortical region of the brain innervated by the targeted cholinergic neurons.

23. (Previously Presented) The method according to Claim 22, wherein each delivery site is preselected by correlating sites of potential loss of cortical fiber density to potential impairment of neurological function in the brain.

24. (Previously Presented) The method according to Claim 23, wherein the cortical region of the brain is the insular or temporal cortex.

25. (Previously Presented) The method according to Claim 22, wherein the stimulation occurs in the cingulate, frontal, entorhinal or hippocampal cortices.

26. (Previously Presented) The method according to Claim 21, wherein the stimulation occurs in the cholinergic forebrain.

27. (Previously Presented) The method according to Claim 22 or 26, wherein the region of the brain containing the targeted neurons is the striatum.

28. (Previously Presented) The method according to Claim 26, wherein the treated mammal is a human with Alzheimer's Disease.

29. (Previously Presented) The method according to Claim 1, wherein the targeted neurons are dopaminergic neurons.

30. (Previously Presented) The method according to Claim 29, wherein the stimulation occurs in dopaminergic neurons innervating the substantia nigra.

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31. (Previously Presented) The method according to Claim 30, wherein the region of the brain containing the targeted dopaminergic neurons is the striatum.

32. (Previously Presented) The method according to Claim 29, wherein the treated mammal is a human with Parkinson's Disease.

33. (Cancelled)

34. (Currently Amended) The method according to ~~Claims~~ Claim 1 or 33, wherein the growth factor-encoding transgene composition is delivered directly by introduction of a transgene-expressing recombinant expression vector into the preselected delivery sites.

35. (Previously Presented) The method according to Claim 34, wherein the transgene-expressing recombinant expression vector is a viral vector.

36. (Previously Presented) The method according to Claim 35, wherein the viral vector is delivered in a pharmaceutically acceptable composition, and provides from 10^{10} to 10^{12} viral particles/ml of composition.

37. (Currently Amended) The method according to ~~Claims~~ Claim 1 or 33, wherein the mammal is a human and the transgene encodes a human ~~nervous system growth factor~~ NGF or GDNF molecule.

38. (Currently Amended) The method according to Claim 37, wherein the transgene encodes human nerve growth factor (NGF).

39. (Cancelled)

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40. (Currently Amended) The method according to Claim 37, wherein the transgene encodes human glial derived nerve growth factor (GDNF).

41. (Cancelled)

42. (Cancelled)

43. (Cancelled)

44. (Previously Presented) The method according to Claim 35, wherein the viral vector is an adeno-associated viral vector.

45. (Previously Presented) The method according to Claim 35, wherein the viral vector is a lentiviral vector.

46. (Previously Presented) The method according to Claim 1, wherein the mammal is a human with aging-related impairment.